Case report

Interferon-α treatment for acute myelitis and intestinal involvement in severe Behçet’s disease

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Case report

A 40-year-old HIV-negative Greek woman was admitted to the Department of Neurology at the University Medical Center of Patras with a 4-day history of progressive muscle weakness in her legs, accompanied by fever (39.5°C), diarrhea and urine retention and a 6-year history of oral and genital lesions that had relapsed 20 days prior to admission. Physical examination revealed multiple large aphthous lesions in the oral mucosa, extensive and deep anogenital ulcers, pseudofolliculitis and pathergy signs but no evidence of arthritis. Initial neurological examination showed muscle power grade 3/5 [Medical Research Council (MRC) scale] in the proximal and grade 4/5 in the distal muscles, brisk symmetrical tendon reflexes, extensor plantar response bilaterally, severe suppression of vibration sense below the knees (particularly on the right extremity) and bilateral reduction of pain appreciation below the T5 level. Neurological disability score in the expanded disability status scale (EDSS) was 6.5, indicating that bilateral assistance was required to walk 20 m. Cranial nerves and motor and sensory function of upper limbs were normal. Magnetic resonance imaging (MRI) of thoracic spinal cord revealed a long intramedullar lesion extending from C7 to T7 vertebrae with gadolinium-enhancement at T3–T4 level, whereas that of the brain showed three unenhanced small lesions at the brainstem (Figure 1). Cerebrospinal fluid analysis revealed 60 lymphocytes/ml, normal protein and glucose content and negative oligoclonal bands. Ophthalmologic investigation disclosed posterior uveitis and spotty hemorrhagic foci on both eyes, whereas colonoscopy showed multiple deep ulcers along the large bowel. Erythrocyte sedimentation rate was 70 mm/h, HLA B51 was positive, whereas serum protein electrophoresis revealed a decrease in albumin and an increase in alpha 1 and 2 globulins. All other biochemical, haematological and serological tests were either negative or within normal limits. Since the patient fulfilled the criteria of the International Study Group for Behçet’s disease, the diagnosis of Behçet’s disease (BD) was established. The pre-treatment clinical severity score of the patient calculated according to Krause et al. was 10 points.

The patient was initially treated with intravenous methylprednisolone pulse therapy (500 mg/day for 5 days) followed by oral 48 mg/day methylprednisolone on a 3-week oral tapering-off scheme. In view of our impressive therapeutic results with interferon-α (IFN-α) monotherapy in a patient with neuro-Behçet and of those reported by Çalışüneri et al. with IFN-α combined with steroids+cyclophosphamide in a BD patient with transverse myelitis initially unresponsive to high-dose steroids, we decided to additionally apply IFN-α (Roferon; Roche Hellas, Athens, Greece) at a dose of 3 x 10^6 IU/day, 3 times/week subcutaneously. However, after 13 days of combined treatment the patient’s...
neurological, intestinal and ocular manifestations revealed no significant change, whereas a massive progression of her mucocutaneous lesions led to her transfer to the Department of Dermatology where the IFN-\(\alpha\) dose was increased to \(6 \times 10^6\) IU/day, 3 times/week. Already 9 days after this increase of IFN dosage there was an impressive improvement of the oral aphthous lesions, the anogenital and the intestinal ulcers, whereas a complete remission of the ophthalmological findings and a dramatic response of myelitis were observed. The patient was able to walk unaided and her pain sense was normalized. EDSS score was 1.5 indicating absence of disability but minimal signs of motor and sensory dysfunction. After 4 weeks of monotherapy with this IFN-\(\alpha\) dosage the oral aphthous lesions, the anogenital and the intestinal ulcers revealed a complete remission, whereas after 6 further weeks of IFN-\(\alpha\) monotherapy all neurological manifestations including urine retention had disappeared (EDSS score 0). Repeated MRI of thoracic spine showed an impressive reduction of the intramedullar non-enhanced lesion (restricted from T2 to T5). Apart from flu-like syndrome (fever, chills and arthralgia) and transient leukopenia during IFN-\(\alpha\) monotherapy no side effects were observed. After complete remission of all clinical manifestations, the patient received a maintenance IFN-\(\alpha\) dosage (\(3 \times 10^6\) IU/day, 2 times/week) over a period of 8 months and then the IFN-\(\alpha\) administration was discontinued. She has presently completed a 12-month drug-free follow-up without any relapse of her mucocutaneous, neurological, intestinal and ocular manifestations.

**Discussion**

A wide spectrum of therapeutic agents has been employed over the years in the management of BD with varying success.\(^6,7\) Tsambaos et al.\(^8\) were the first to introduce the systemic application of IFN-\(\alpha\) in the treatment of BD. Their impressive therapeutic results were confirmed in a large number of subsequent clinical trials.\(^9\)–\(^14\) Thus, IFN-\(\alpha\) is presently regarded as a highly effective, safe and well tolerated form of therapy, particularly with regard to mucocutaneous manifestations.

**Figure 1.** Magnetic resonance scan of the thoracic cord (sagittal T1-weighted images with gadolinium) showing the intramedullary enhanced lesion before (left image) and 1 month after treatment (right image).
and ocular manifestations of BD. This has been confirmed in the patient presented herein, in which administration of IFN-α—despite tapering of steroids—led within 9 days to a complete remission of posterior uveitis and to an impressive improvement of the mucocutaneous lesions, which completely disappeared after 4 weeks of monotherapy with this cytokine. In view of the sparse data about the therapeutic effects of IFN-α on acute myelitis and intestinal involvement in BD, we will mainly concern ourselves herein with the discussion about the therapeutic response of these manifestations in our patient.

Transverse myelitis is a clinical syndrome characterized by an inflammatory process affecting the full width of spinal cord that leads to varying degrees of motor, sensory and autonomic dysfunction below the level of the lesion. It is reportedly observed in 4–14% of patients with neuro-Behçet but its occurrence as the sole neurological manifestation of BD is rare. Combined administration of systemic corticosteroids and immunosuppressants with or without colchicine, is the most commonly applied regimen in the management of transverse myelitis in BD; however, the efficacy of this therapeutic modality is far from being satisfactory; additionally, its use is associated with serious side effects. A favourable therapeutic response of neurological manifestations has been reported in BD patients treated with IFN-α, either as monotherapy or in combination with colchicine or steroids. Our group has shown that IFN-α administration to a patient with intractable epilepsy as the sole manifestation of neuro-Behçet resulted in a complete and persistent cessation of seizures despite discontinuation of all antiepileptic agents. A BD patient with transverse myelitis initially unresponsive to high-dose steroids revealed a favourable response to the combined administration of steroids+cyclophosphamide with a high dosage of IFN-α. In the patient presented herein, a 13-day combined treatment with high-dose steroids and low-dose IFN-α had no effect on myelitis; nevertheless, increase of IFN-α dosage, suggesting that this well-tolerated cytokine may be solely or at least predominantly responsible for the observed complete resolution of myelitis, intestinal disease and of the other severe clinical manifestations in our BD patient. Our findings suggest that IFN-α may be a highly effective, safe and well-tolerated form of therapy not only for severe mucocutaneous and ocular manifestations of BD but also for acute myelitis and intestinal ulcers. Undoubtedly, further studies on large numbers of patients are required to validate the efficacy and safety of IFN-α monotherapy as a possible first line option in the management of intestinal and neurological involvement and other severe manifestations in patients with BD.

Conflict of interest: None declared.

References


